

PATENT

Attorney Docket No. 22903XA-T

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of:

Joseph P. Steiner, et al.

Serial No.: not assigned

Filing Date: February 16, 2001

For: SMALL MOLECULE PIPECOLIC ACID DERIVATIVE HAIR
GROWTH COMPOSITIONS AND USES

PRELIMINARY AMENDMENT

Commissioner for Patents
Washington, D.C. 20231

Sir:

Before action in the captioned application and before
calculation of the filing fee, please amend the captioned
application as follows:

IN THE SPECIFICATION

Please amend the specification by replacing the first sentence
thereof with the following:

--This application is a divisional application of U.S.
Patent Application Serial No. 09/089,373, filed on June
3, 1998, now U.S. Patent No. 6,191,125, granted February
20, 2001, the entire contents of which is incorporated by
reference herein as though set forth in full.--

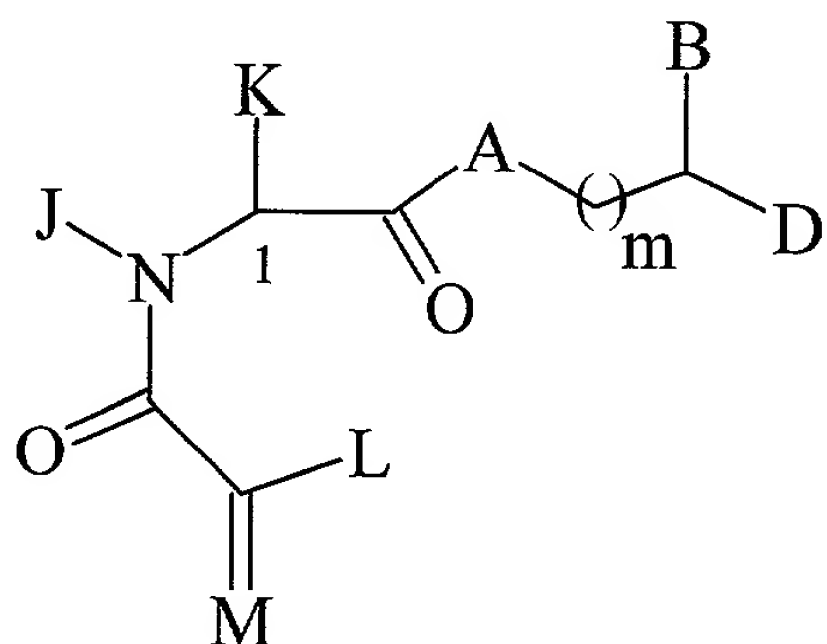
IN THE CLAIMS

Please cancel claims 1-4, which were allowed, as amended, in U.S. Patent Application Serial No. 09/089,373. Please cancel claim 7 without prejudice or disclaimer of the subject matter therein.

Please amend the claims as follows:

5. (Once amended) A pharmaceutical composition which comprises:

- (i) an effective amount of a compound [pipecolic acid derivative] for treating alopecia or promoting hair growth in an animal in need thereof, wherein said compound is [the pipecolic acid derivative is a compound] of formula I



or a pharmaceutically acceptable salt, ester, or solvate thereof, wherein:

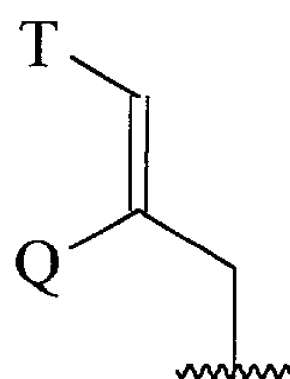
A is [CH₂,] O, NH, or N-(C₁-C₄ alkyl);

B and D are independently Ar, C₅-C₇ cycloalkyl substituted C₁-C₆

straight or branched chain alkyl or C₂-C₆ straight or branched chain alkenyl, C₅-C₇ cycloalkenyl substituted C₁-C₆ straight or branched chain alkyl or C₂-C₆ straight or branched chain alkenyl, or Ar substituted C₁-C₆ straight or branched chain alkyl or C₂-C₆ straight or branched chain alkenyl,

wherein in each case, one or two carbon atom(s) of said alkyl or alkenyl [may be] is/are optionally substituted with one or two heteroatom(s) independently selected from the group consisting of oxygen, sulfur, SO, and SO₂ [in chemically reasonable substitution patterns],

or B and D are independently the fragment



wherein Q is hydrogen, C₁-C₆ straight or branched chain alkyl or C₂-C₆ straight or branched chain alkenyl; and

T is Ar or C₅-C₇ cycloalkyl substituted at positions 3 and 4 with substituents independently selected from the group consisting of hydrogen, hydroxy, O-(C₁-C₄ alkyl), O-(C₂-C₄ alkenyl), and carbonyl;

Ar is selected from the group consisting of 1-naphthyl, 2-

napthyl, 2-furyl, 3-furyl, 2-thienyl, 3-thienyl, 2-pyridyl, 3-pyridyl, 4-pyridyl and phenyl, monocyclic and bicyclic heterocyclic ring systems with individual ring sizes being 5 or 6 which [contain] have in either or both rings a total of 1-4 heteroatoms independently selected from oxygen, nitrogen and sulfur, [;]

wherein Ar [contains] has 1-3 substituent(s) independently selected from the group consisting of hydrogen, halo, hydroxy, hydroxymethyl, nitro, CF₃, trifluoromethoxy, C₁-C₆ straight or branched chain alkyl, C₂-C₆ straight or branched chain alkenyl, O-(C₁-C₄ straight or branched chain alkyl), O-(C₂-C₄ straight or branched chain alkenyl), O-benzyl, O-phenyl, amino, 1,2-methylenedioxy, carbonyl, and phenyl;

L is either hydrogen or U; M is either oxygen or CH-U, provided that if L is hydrogen, then M is CH-U, or if M is oxygen then L is U;

U is hydrogen, O-(C₁-C₄ straight or branched chain alkyl), O-(C₂-C₄ straight or branched chain alkenyl), C₁-C₆ straight or branched chain alkyl, C₂-C₆ straight or branched chain alkenyl, C₅-C₇ cycloalkyl, C₅-C₇ cycloalkenyl substituted with C₁-C₄ straight or branched chain alkyl or C₂-C₄ straight or branched chain alkenyl, (C₁-C₄ alkyl or C₂-C₄ alkenyl)-Ar, or Ar;

J is hydrogen, C₁ or C₂ alkyl, or benzyl; K is C₁-C₄ straight

or branched chain alkyl, benzyl or cyclohexylmethyl; or J and K are taken together to form a [5-] 7 membered heterocyclic ring which is substituted with oxygen, sulfur, SO, or SO₂;

[n] m is 0-3; and

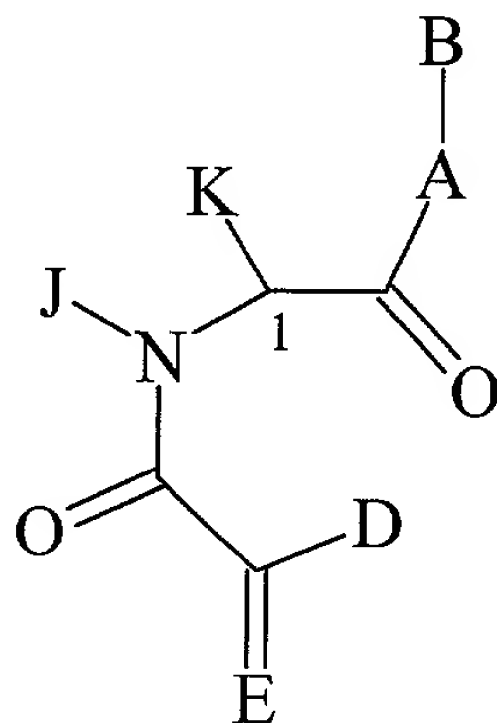
said [pipecolic acid derivative] compound has an affinity for FKBP-type immunophilins; [and]

(ii) a second hair revitalizing agent; and

(iii) a pharmaceutically acceptable carrier.

6. (Once amended) A pharmaceutical composition which comprises:

(i) an effective amount of a compound [pipecolic acid derivative] for treating alopecia or promoting hair growth in an animal in need thereof, wherein said compound is [the pipecolic acid derivative is a compound] of formula II

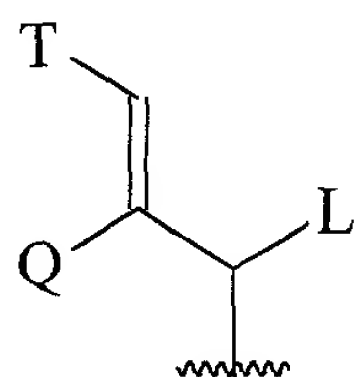


II

or a pharmaceutically acceptable salt, ester, or solvate thereof,
wherein:

A is O, NH, or N-(C₁-C₄ alkyl);

B is hydrogen, CHL-Ar, C₁-C₆ straight or branched chain alkyl,
C₂-C₆ straight or branched chain alkenyl, C₅-C₇ cycloalkyl, C₅-C₇
cycloalkenyl, Ar substituted C₁-C₆ alkyl or C₂-C₆ alkenyl, or



wherein L and Q are independently hydrogen, C₁-C₆
straight or branched chain alkyl, or C₂-C₆ straight or
branched chain alkenyl; and

T is Ar or C₅-C₇ cyclohexyl substituted at positions
3 and 4 with substituents independently selected from the
group consisting of hydrogen, hydroxy, O-(C₁-C₄ alkyl),
O-(C₂-C₄ alkenyl), and carbonyl;

Ar is selected from the group consisting of 1-
naphthyl, 2-naphthyl, 2-furyl, 3-furyl, 2-thienyl, 2-
pyridyl, 3-pyridyl, 4-pyridyl, and phenyl, having 1-3
substituent(s) independently selected from the group
consisting of hydrogen, halo, hydroxy, nitro, CF₃, C₁-C₆
straight or branched chain alkyl, C₂-C₆ straight or
branched chain alkenyl, O-(C₁-C₄ straight or branched

chain alkyl), O-(C₂-C₄ straight or branched chain alkenyl), O-benzyl, O-phenyl, amino, and phenyl; [.]

D is hydrogen or U; E is oxygen or CH-U, provided that if D is hydrogen, then E is CH-U, or if E is oxygen, then D is U;

U is hydrogen, O-(C₁-C₄ straight or branched chain alkyl), O-(C₂-C₄ straight or branched chain alkenyl), C₁-C₆ straight or branched chain alkyl, C₂-C₆ straight or branched chain alkenyl, C₅-C₇-cycloalkyl, C₅-C₇ cycloalkenyl substituted with C₁-C₄ straight or branched chain alkyl or C₂-C₄ straight or branched chain alkenyl, 2-indolyl, 3-indolyl, (C₁-C₄ alkyl or C₂-C₄ alkenyl)-Ar, or Ar;

J is hydrogen, C₁ or C₂ alkyl, or benzyl; K is C₁-C₄ straight or branched chain alkyl, benzyl or cyclohexylethyl; or J and K are taken together to form a [5-] 7 membered heterocyclic ring which is substituted with oxygen, sulfur, SO, or SO₂; and

said compound has an affinity for FKBP-type immunophilins;

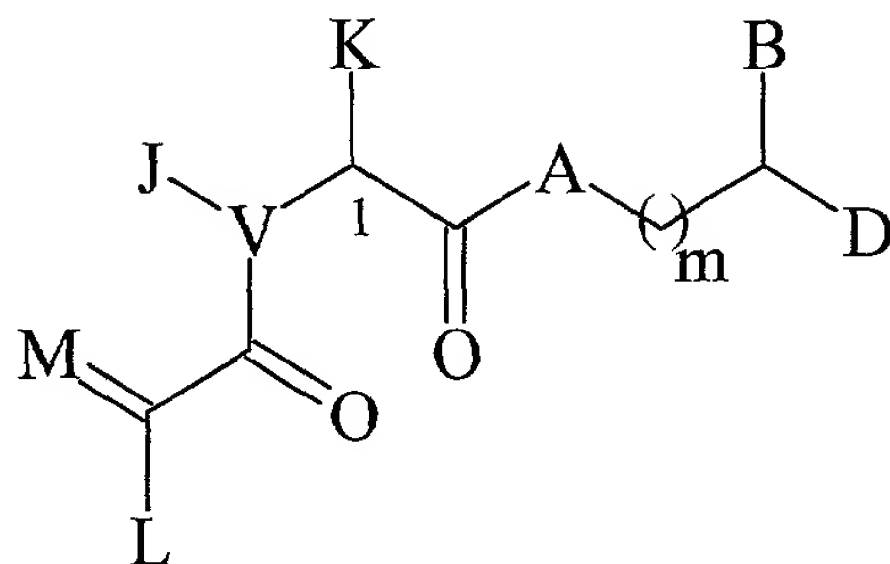
(ii) a second hair revitalizing agent; and

(iii) a pharmaceutically acceptable carrier.

8. (Once amended) A pharmaceutical composition which comprises:

(i) an effective amount of a compound [pipecolic acid derivative] for treating alopecia or promoting hair growth in an animal in need thereof, wherein said

compound is [the pipecolic acid derivative is a compound]
of [formula] formula IV



IV

or a pharmaceutically acceptable salt, ester, or solvate thereof,
wherein:

V is C, N, or S;

J and K, taken together with V and the carbon atom to which they are respectively attached, form a [5-] 7 membered saturated or unsaturated heterocyclic ring [containing] having, in addition to V, one or more heteroatom(s) selected from the group consisting of O, S, SO, SO₂, N, NH, and NR;

R is either C₁-C₉ straight or branched chain alkyl, C₂-C₉ straight or branched chain alkenyl, C₃-C₉ cycloalkyl [cycloalkyl], C₅-C₇ cycloalkenyl, or Ar₁,

wherein R is either unsubstituted or substituted with one or more substituent(s) independently selected from the group consisting of halo, haloalkyl, carbonyl, carboxy, hydroxy, nitro, trifluoromethyl, C₁-C₆ straight or

branched chain alkyl, C₂-C₆ straight or branched chain alkenyl, C₁-C₄ alkoxy, C₂-C₄ alkenyloxy, phenoxy, benzyloxy, thioalkyl, alkylthio, sulfhydryl, amino, alkylamino, aminoalkyl, aminocarboxyl, and Ar₂;

Ar₁ and Ar₂ are independently an alicyclic or aromatic, mono-, bi- or tricyclic, carbo- or heterocyclic ring, [;]

wherein the individual ring size is 5-8 members, [;]

wherein said heterocyclic ring has [contains] 1-6 heteroatom(s) independently selected from the group consisting of O, N, and S;

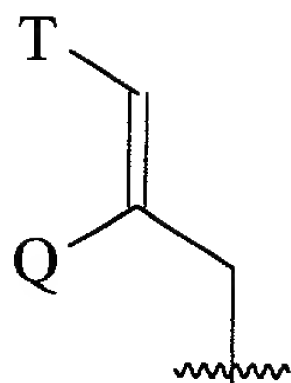
[A, B, D, L, M, and m are as defined in claim 5 above;]

A is O, NH, or N-(C₁-C₄ alkyl);

B and D are independently Ar, C₅-C₇ cycloalkyl substituted C₁-C₆ straight or branched chain alkyl or C₂-C₆ straight or branched chain alkenyl, C₅-C₇ cycloalkenyl substituted C₁-C₆ straight or branched chain alkyl or C₂-C₆ straight or branched chain alkenyl, or Ar substituted C₁-C₆ straight or branched chain alkyl or C₂-C₆ straight or branched chain alkenyl,

wherein in each case, one or two carbon atom(s) of said alkyl or alkenyl is/are optionally substituted with one or two heteroatom(s) independently selected from the group consisting of oxygen, sulfur, SO, and SO₂,

or B and D are independently the fragment



wherein Q is hydrogen, C₁-C₆ straight or branched chain alkyl or C₂-C₆ straight or branched chain alkenyl; and

T is Ar or C₅-C₇ cycloalkyl substituted at positions 3 and 4 with substituents independently selected from the group consisting of hydrogen, hydroxy, O-(C₁-C₄ alkyl), O-(C₂-C₄ alkenyl), and carbonyl;

Ar is selected from the group consisting of 1-naphthyl, 2-naphthyl, 2-furyl, 3-furyl, 2-thienyl, 3-thienyl, 2-pyridyl, 3-pyridyl, 4-pyridyl, phenyl, and monocyclic and bicyclic heterocyclic ring systems with individual ring sizes being 5 or 6, which have in either or both rings a total of 1-4 heteroatoms independently selected from oxygen, nitrogen and sulfur,

wherein Ar has 1-3 substituent(s) independently selected from the group consisting of hydrogen, halo, hydroxy, hydroxymethyl, nitro, CF₃, trifluoromethoxy, C₁-C₆ straight or branched chain alkyl, C₂-C₆ straight or branched chain alkenyl, O-(C₁-C₄ straight or branched chain alkyl), O-(C₂-C₄ straight or branched chain

alkenyl), O-benzyl, O-phenyl, amino, 1,2-methylenedioxy,
carbonyl, and phenyl;

L is either hydrogen or U; M is either oxygen or CH-U,
provided that if L is hydrogen, then M is CH-U, or if M is oxygen
then L is U;

U is hydrogen, O-(C₁-C₄ straight or branched chain alkyl), O-
(C₂-C₄ straight or branched chain alkenyl), C₁-C₆ straight or
branched chain alkyl, C₂-C₆ straight or branched chain alkenyl, C₅-C₇
cycloalkyl, C₅-C₇ cycloalkenyl substituted with C₁-C₄ straight or
branched chain alkyl or C₂-C₄ straight or branched chain alkenyl,
(C₁-C₄ alkyl or C₂-C₄ alkenyl)-Ar, or Ar; and

m is 0-3; [and]

(ii) a second hair revitalizing agent; and

(iii) a pharmaceutically acceptable carrier.

REMARKS

Upon entry of the above amendments, claims 5, 6, and 8 are pending in the application. Canceled claims 1-4 were allowed, as amended, in U.S. Patent Application Serial No. 09/089,373. The amendments do not introduce new matter within the meaning of 35 U.S.C. §132. Basis for the amendments is found at page 26, lines 5-9, as well as claims 5, 6, and 8 as originally filed, and elsewhere throughout the specification and claims. Accordingly,

the Examiner is respectfully requested to enter the above
amendments before examination.

The Examiner is welcomed to telephone the undersigned attorney
if (s)he has any questions or comments.

Respectfully submitted,

NATH & ASSOCIATES PLLC

Date: February 16, 2001

NATH & ASSOCIATES

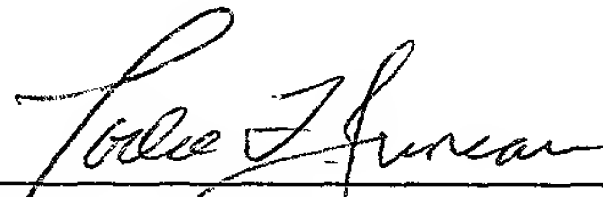
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